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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,164	08/31/2006	Josef Constantin Szeles	SZELES-5 PCT	4621

25889 7590 10/28/2009

COLLARD & ROE, P.C.
1077 NORTHERN BOULEVARD
ROSLYN, NY 11576

EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1619	

MAIL DATE	DELIVERY MODE
10/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,164	SZELES, JOSEF CONSTANTIN	
	Examiner	Art Unit	
	SHANON A. FOLEY	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-5,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/06 and 8/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on July 20, 2009 is acknowledged. The traversal is on the ground(s) that there is no unreasonably burdensome search required for all of the inventions. In addition, applicant points out the extra expenses accrued due to filing multiple applications.

The reasons for traversal have been fully considered, but are not found persuasive because the instant application is a national stage of an international application filed under 35 U.S.C. 371 and is subject to unity of invention practice under 37 CFR 1.499, see the MPEP § 1896. As such, search burden is not a criterion for establishing a lack of unity between inventions for internationally filed applications. However, due to the complex nature of all of the inventions claimed, a search for each and every invention would pose an undue search burden. In addition, extra expense is also not a criterion for considering unity of invention or independent and distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-5, 25 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 20, 2009. Claims 6-24 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 4, 2006 and August 31, 2006 have been considered by the examiner.

Claim Objections

Claims 15 and 16 are objected to because of the following informalities: In both claims, the last two words of each claim, i.e., "takes place", is redundant. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 7, 10, 15 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Malin et al. (US 5,084,007).

Malin et al. anticipate a method of punctual stimulation therapy with an electrical current supplied with needle electrodes stuck into the skin while intravenously infusing 100-500 mg/kg of D-phenylalanine, a substance that inhibits enzymatic decomposition of endogenous opioids, see column 2, lines 59-62; column 14, lines 43-46; column 16, Examples 7 and 8 and claims 1, 2, 4, 9 and 13. Malin et al. also anticipate simultaneous intravenous infusion and electrostimulation for 20 minutes, see column 14, lines 44-49. The punctual electrostimulation method of Malin et al. is carried out by insertion of needle electrodes stuck in both ears, see column 8, lines 41-49 and column 9, lines 28-33 in Example 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al. and Blum (US 6,955,873).

See the teachings of Malin et al. above. Malin teach a combination of D-phenylalanine and D-leucine amino acids present in the central nervous system, see column 6, lines 31-33. Malin et al. also teach intravenous infusion of D-phenylalanine with other amino acids in Examples 7 and 8, bridging columns 16-17 and claim administering a combination of amino acids in the electrostimulation method, see claims 1 and 2. However, Malin et al. do not specifically teach intravenous infusion with D- phenylalanine and D-leucine amino acids.

Blum teaches intravenous infusion of D-phenylalanine and D-leucine amino acids, see column 68, lines 37-67.

One of ordinary skill in the art at the time the invention was made would have been motivated to intravenously infuse both D-phenylalanine and D-leucine amino acids because Blum teaches that the combination of these two amino acids in humans are known to evoke a long-lasting analgesic effect, providing pain relief close to that approaching morphine, see column 5, lines 16-23. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of combining the D-phenylalanine and D-leucine amino acid infusion of Blum in the method of Malin et al. because both of the references teach infusing a combination of amino acids during punctual stimulation therapy to ease pain, see Examples 7 and 8 and claims 1 and 2 of Malin et al. and column 35, lines 46-50 and column 64, lines 25-37 of Blum.

While Malin et al. teach infusing 100-500 mg/kg of D-phenylalanine in combination with electrostimulation treatment, see Examples 7 and 8, bridging columns 16 and 17, Malin et al. do not teach or suggest delivering a concentration of D-phenylalanine in concentration of at least 5 g/L.

However, Blum teaches administering a solution of D-phenylalanine in a concentration of at least 5 g/L, see column 69, lines 21-25.

One of ordinary skill in the art at the time the invention was made would have been motivated to adjust the concentration of D-phenylalanine of Malin et al. to at least 5 g/L of Blum to ensure inhibition of enkephalinases, endorphinases and dyorphynases, see column 69, lines 21-25 of Blum. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for optimizing the quantity of D-phenylalanine infused in the method of Malin et al. and Blum since adjustment of an administered dose is well within the purview for one of ordinary skill in the art considering the individual parameters of each patient treated.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al. and Hermelin et al. (US 6,197,329).

See the teachings of Malin et al. above. Malin et al. do not teach administering an anti-emetic.

Hermelin et al. teach administering an anti-emetic to alleviate nausea, see column 5, lines 51-60.

One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the anti-emetic of Hermelin et al. in the method of Malin et al. to

relieve symptoms of nausea due to withdrawal from a drug addiction, see claims 20 and 21 of Malin et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of combining the anti-emetic of Hermelin et al. in the method of Malin et al. because Hermelin et al. also teach acupressure, a derivative of acupuncture, as a means to alleviate nausea, see column 14, lines 35-44.

Claims 13, 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al. and Ehrenpreis et al. (US 4,439,452).

See the teachings of Malin et al. above. Malin et al. teach simultaneous intravenous infusion and electrostimulation for 20 minutes, see column 14, lines 44-49. In addition, Malin et al. also teach treatments in consecutive days of transcranial electrostimulation (TE) to treat nicotine withdrawal symptoms in Example 19, bridging columns 20-21 and concomitant treatment regiments of infusion and TE, see claims 9, 14, 20 and 21 for example. However, Malin et al. do not teach duration of infusion lasting at least one hour or 2-3 hours or administering the infusion for consecutive days.

Ehrenpreis et al. teach infusing D-phenylalanine for 2-3 hours to alleviate inflammation and pain, see column 8, lines 7-25 and over a period of consecutive days, see column 5, lines 16-18 and Table 5.

One of ordinary skill in the art at the time the invention was made would have been motivated to increase the time of infusion in the method of Malin et al. to maximize the pain relief and reduce inflammation, see column 8, lines 7-25 and Table 5 of Ehrenpreis et al. One of ordinary skill in the art at the time the invention was made would have been further motivated to increase time and duration of the infusion of Malin et al. since extended treatment, even at high

doses of D-phenylalanine, does not present side-effects, tolerance or addiction, see column 5, lines 39-53; column 6, lines 3-5 and column 7, lines 22-23. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of increasing the duration of infusion, taught by Ehrenpreis et al., in the method of Malin et al. since both references teach ameliorating pain and inflammation with a combination of D-phenylalanine and other amino acids that inhibit the destruction of endogenous opioids, see claims 1-5 and 12-14 of Ehrenpreis et al. and claims 1-3, 9 and 13 of Malin et al.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al.

Malin et al. teach beginning intravenous infusion 5 minutes before electrostimulation in column 15, lines 16-18. Malin et al. also teach administering neuroactive chemical promoters, such as D-phenylalanine and –hydroxy-dl-tryptophan 30 minutes prior to electrical stimulation, see column 13, lines 20-31 and column 15, lines 52-64. In column 14, lines 44-49, column 17, lines 34-41 and claim 9, Malin et al. teach concomitantly administering a neuroactive chemical promoter, such as D-phenylalanine, and transcranial electrostimulation.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the intravenous infusion at least 20 minutes before beginning transcranial electrostimulation and continuing the infusion during stimulation treatment since both regiments taught by Malin et al. resulted in the most enhanced analgesic effects, see Figure 2 and 3.

Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al. and Ehrenpreis et al. as applied to claims 6, 7, 10, 13-15 , 17 and 18 above, and further in view of Josefson et al. (Rheumatology. May 2003; 42: 1149-1154).

See the teachings of Malin et al. and Ehrenpreis et al. above. Neither Malin et al. nor Ehrenpreis et al. teach punctual stimulation in one ear followed by or prior to punctual stimulation in both ears.

Josefson et al. teach unilateral or bilateral needle insertion into ears for acupuncture sessions, see the last paragraph of the second column on page 1150. It is noted that the patients of Josefson et al. received multiple acupuncture treatments, see "*Phase 2*", "*Phase 5*" and "*Phase 6*" on page 1151.

Since Josefson et al. teach unilateral or bilateral placement of needles in the ear prior to each acupuncture session, it cannot be precisely determined whether needle placement configuration was alternated between various sessions or remained unilateral or bilateral throughout each treatment. In any case, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have delivered electrostimulatory treatment to ears unilaterally or bilaterally, depending on the individual circumstances of the patient being treated, such as severity of disease/exacerbation and response to treatment, see the paragraph bridging the columns on page 1150 of Josefson et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to vary the electrostimulation from unilateral or bilateral placement in ears since Malin et al. determine an increased analgesic response in a group receiving bilateral electrode placement in ears compared with unilateral electrode placement, see column 11, lines 9-10, 51-55 and column 12, lines 53-55.

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malin et al. and Capel (US4,646,744).

See the teachings of Malin et al. above. Malin et al. do not teach or suggest applying a high frequency of electrostimulation in a range between 50-500 Hz, or applying a high frequency and subsequently or intermittently applying a low frequency.

Capel teaches applying a frequency signal of 100-200 Hz followed by and/or intermittent application of a frequency signal of 10-35 Hz during transcranial electrostimulation, see column 3, line 21 to column 4, line 27 and column 5, line 66 to column 6, line 8.

One of ordinary skill in the art at the time the invention was made would have been motivated to apply a high frequency followed by a low frequency during electro-acupuncture method of Malin et al. to first remove an abused drug from active receptor sites in the brain and promote the production of endogenous neurotransmitters, which replace the drug at the receptor sites, see column 8, lines 14-55. One of ordinary skill in the art at the time the invention was made would have been motivated to apply an intermittent application of a low frequency signal in the method of Malin et al. to eliminate discomfort, see column 2, lines 21-25 and to reduce deleterious polarization effects, see column 9, lines 59-64 of Capel. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the treatment electrostimulation regiments of Capel in the method of Malin et al. because both references teach using transcranial electrostimulation to subdue drug addictions, see claims 20 and 21 of Malin et al. and column 7, lines 24-28 of Capel.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANON A. FOLEY whose telephone number is (571)272-

0898. The examiner can normally be reached on flex, generally M-F 7AM - 3 PM, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shanon A. Foley/
Primary Examiner
Art Unit 1619